Computed Tomography in Cases of Coccidioidal Meningitis, With Clinical Correlation

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Cranial computed tomographic (CT) scans of 22 patients with coccidioidal meningitis were reviewed and their clinical course was analyzed. Abnormalities of the ventricular system or the basilar cisterns or both were present in 16 instances. Although it is not a definitive diagnostic tool, the CT scan is helpful in suggesting a diagnosis of coccidioidal meningitis and in predicting the prognosis of patients affected by the disease.

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Coccidioidal meningitis is a fungal infection affecting visitors to and residents of the southwestern United States. Although the disease is relatively rare, it is a source of considerable mortality and morbidity when it occurs. The initial signs and symptoms of coccidioidal meningitis are often nonspecific and may be unaccompanied by a history of systemic infection, thereby delaying early diagnosis and treatment. We undertook a retrospective analysis of cranial computed tomographic (CT) scans in patients with coccidioidal meningitis to determine whether this test is capable of providing useful information regarding diagnosis, treatment or prognosis.

Methods

Cranial CT scans of 22 patients diagnosed as having coccidioidal meningitis at the Barrow Neurological Institute from 1975 to 1981 were reviewed. Scans were done on either an upgraded EMI Mark I scanner or a Delta 2020 scanner. Contrast enhancement by drip infusion was carried out in 17 patients. All scans were interpreted by a neuroradiologist (R.A.F.) who did not know the patients' clinical status. The scans were evaluated for hypodense or hyperdense areas, the presence of hydrocephalus (generalized or compartmentalized) and cisternal integrity.

Patients with coccidioidal meningitis ranged in age from 2 to 80 years, with a mean of 39 years. There were 15 male and 7 female patients. Six patients were white, three were Mexican-American, three were American Indian, one was Filipino and one was black; in eight instances race was not specified. In all patients cerebrospinal fluid specimens showed positive coccidioidal complement fixation titers, which were reactive at 1:4 or greater. Of the 22 patients, 12 (55%) who had meningitis had no previous history of a coccidioidal infection. The neurologic state of patients at the time of their first CT scan was documented by hospital chart review. Follow-up information was obtained through a questionnaire and by review of recent charts.

All patients received amphotericin B intrathecally. Other therapeutic modalities used in selected instances included systemic amphotericin B, systemic or intrathecal isonidazole compounds and ventricular shunting. A full discussion of the diagnosis and treatment of coccidioidal meningitis is beyond the scope of this paper and has been covered elsewhere.[1-5]

Results

Of 22 patients, 6 (27%) with coccidioidal meningitis were felt to have normal CT scans at the time of initial diagnosis. Scans of the remaining patients (73%) showed single or combined abnormalities in ventricular size, basal cisterns or brain parenchyma (Table 1).

The ventricular system was enlarged in either a generalized or an asymmetric fashion in 15 of 22 patients (Table 2). Seven of these patients had diffuse ventriculomegaly affecting the lateral, third and fourth ventricles in equal degree. An example of this type of abnormality is seen in Figure 1. The remaining patients had compartmentalized hydrocephalus. Examples of asymmetric ventricular enlargement in cases of coccidioidal meningitis are shown in Figure 2.

Enhancement or obliteration, or both, of the basal cisterns was the second most common abnormality seen on CT scan and was present in 12 patients (55%). One patient had cis-

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TABLE 1.—*Computed Tomographic Scan Findings in 22 Patients With Coccidioidal Meningitis**

Findings	*No. of Patients*
Normal	6
Ventricular dilatation	15
Cisternal obliteration	5
Cisternal enhancement	3
Cisternal obliteration and enhancement	4
Hypodense white matter lesions	2
Ependymal enhancement	1

*Of the 16 patients who had abnormal findings on scans, some had several abnormal features (see text for more details).

TABLE 2.—*Patterns of Ventricular Dilatation in 15 Patients With Coccidioidal Meningitis*

Ventricular Dilatation	*No. of Patients*
Generalized	7
Large lateral and third ventricles plus	
Nonvisualized fourth ventricle	2
Mildly dilated fourth ventricle	2
Greatly dilated fourth ventricle	3
Asymmetric dilatation of the temporal horn	1

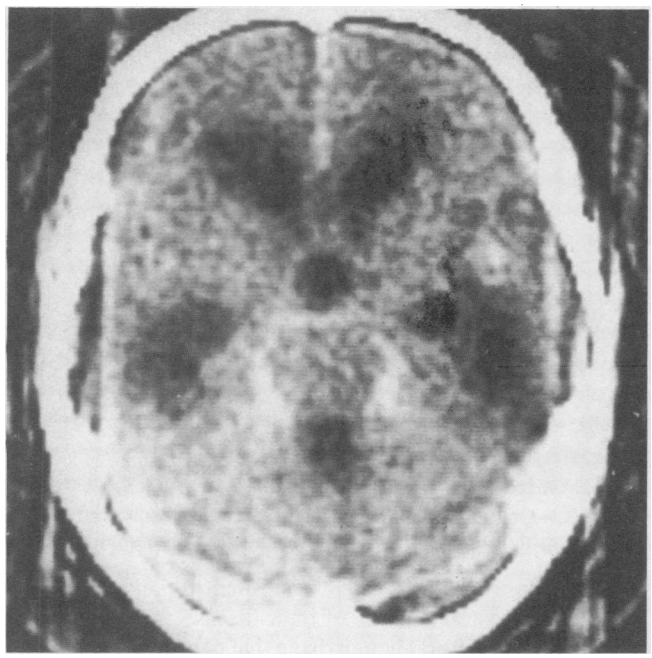

Figure 1.—Computed tomographic scan showing generalized (symmetric) dilatation of the ventricular system. Note the enhancement of the basal cisterns.

ternal involvement with normal-sized ventricles, while the remaining 11 patients had some degree of ventricular enlargement in combination with their cisternal abnormalities. Examples of cisternal abnormalities are shown in Figure 3.

One patient had ependymal enhancement and abnormalities in the cisternal region. Brain parenchymal abnormalities were seen in two patients and consisted of small hypodense areas in the subcortical white matter. There were no instances of hypodense zones within gray matter structures in our series. Hyperdense parenchymal abnormalities such as hemorrhage or calcification were also not encountered.

The clinical state of patients at the time a diagnosis of coccidioidal meningitis was established was correlated with their initial CT scan. Fourteen patients had no focal neurologic deficits but had signs and symptoms of meningeal irritation such as headache, low-grade fever and nuchal rigidity. The remaining eight patients had indications of meningeal irritation but also showed evidence of impaired mentation, personality change, depressed level of consciousness or signs of elevated intracranial pressure. Patients with abnormalities apparent on CT scans were considerably more likely to have evidence of neurologic impairment than those with normal scans. Of 16 persons with a CT scan abnormality at the time of initial diagnosis, 7 (44%) presented with lethargy, confusion or papilledema, compared with one of six patients (17%) with a normal CT scan and a similar clinical picture.

Attempts were also made to correlate long-term clinical outcome with initial CT scan findings. Follow-up data were obtained through December 1981 or up to the time of death in 18 patients. Four patients were lost to follow-up before the completion of our study. In the group with normal CT scans, a single death was recorded in an 80-year-old man who died of a myocardial infarction unrelated to his coccidioidal meningitis. The remaining five patients were alive at the time of the last follow-up and were leading independent lives (average follow-up time, 18 months). There were 5 deaths in the 16

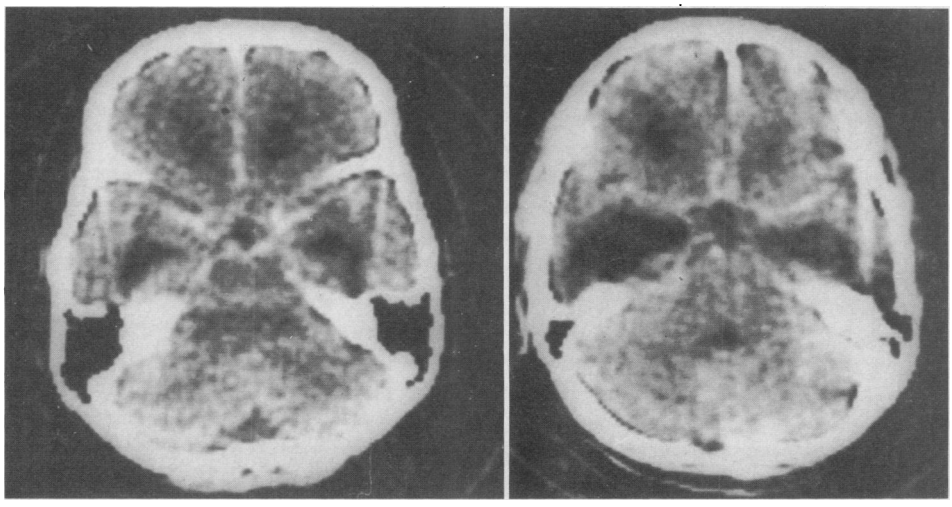

Figure 2.—Compartmentalized (asymmetric) dilatation of the ventricular system. **Left,** There is nonvisualization of the fourth ventricle, and, **Right,** a mildly dilated fourth ventricle.

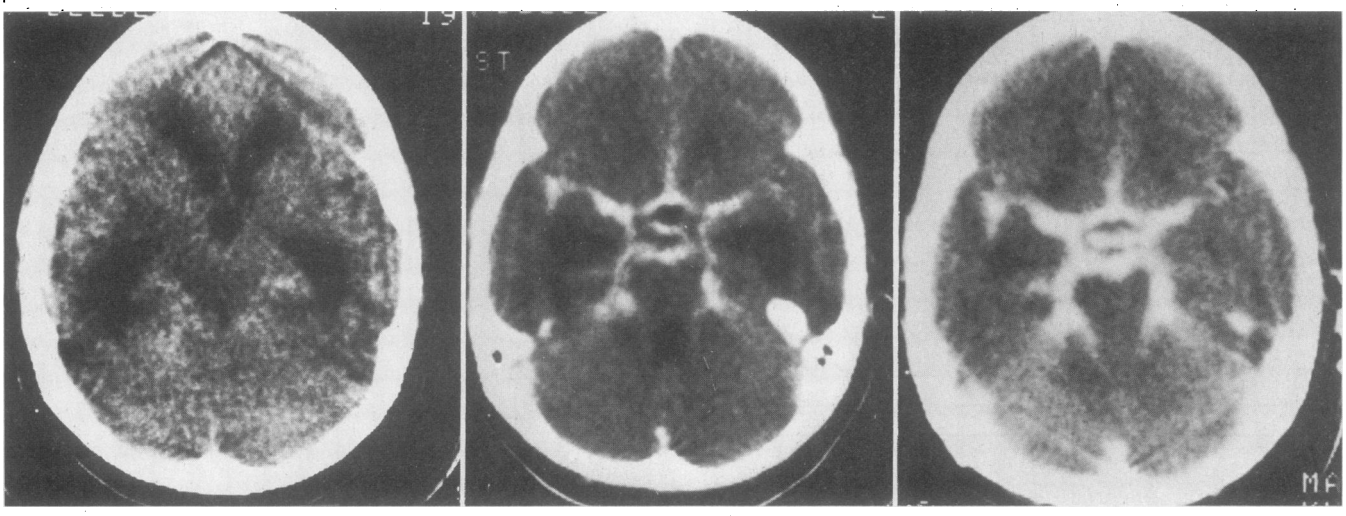

Figure 3.—Obliteration of the basal cisterns, **Left,** followed by cisternal enhancement after intravenous administration of contrast medium, **Middle. Right,** There is striking progression in the magnitude of enhancement at follow-up scan one month later.

patients whose CT scans were abnormal initially. Four patients died of complications of their disease and one patient died of an intracerebral hemorrhage that may have been unrelated to his infection. Of the remaining 11 patients, 5 were functioning independently, 3 were semidependent but resided at home and 3 were totally dependent on nursing-home care (average follow-up time, 34 months). These findings suggest that patients with coccidioidal meningitis whose initial CT scan is normal have a better long-term prognosis than those with ventricular or cisternal CT scan abnormalities at the time a diagnosis is made.

Follow-up CT scans were obtained in a number of cases and were of value in assessing progressive hydrocephalus or the response to ventricular shunting. Two patients were of particular interest in this regard. Both underwent lateral ventricular shunting for generalized ventriculomegaly and symptoms of elevated intracranial pressure. At three and six months postshunting, repeat CT scans showed pronounced enlargement of the fourth ventricle that had not been present initially (Figure 4). This was associated with clinical evidence of posterior fossa hypertension. The possibility of isolated fourth ventricular dilatation in patients with coccidioidal meningitis with lateral ventricular shunts must be kept in mind if posterior fossa symptoms develop. The appropriate diagnosis can be readily established by repeat CT scanning.

Discussion

Coccidioides immitis is a fungal organism endemic to the southwestern United States and to certain regions of Central and South America. It manifests itself most frequently as a benign and self-limited pulmonary infection. However, in less than 1%[3] of affected patients, hematogenous dissemination to the central nervous system may occur. The signs and symptoms of coccidioidal meningitis are meningeal irritation, increased intracranial pressure or impaired mentation. The cerebrospinal fluid will show a fungal or tuberculous meningitis, including nongranulocytic leukocytosis, an elevated protein value and a moderately depressed glucose level. The organism itself is rarely cultured from a spinal fluid specimen and a definitive diagnosis is established by obtaining a positive cerebrospinal fluid complement fixation titer.

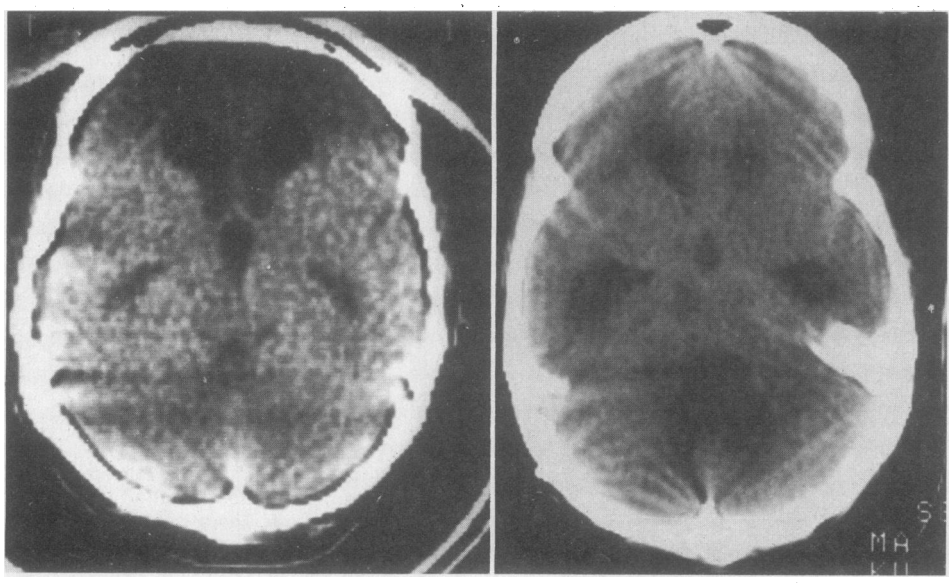

Figure 4.—**Left** and **Right,** Progressive dilatation of the fourth ventricle over a period of ten weeks. A ventriculoperitoneal shunt had been placed during the interim period.

Before the advent of chemotherapy with amphotericin B and ventricular shunting procedures, coccidioidal meningitis was usually fatal within one year of diagnosis.[6] Although these modalities have increased survival times and produced apparent cures in some patients, the disease continues to be associated with substantial mortality and morbidity.

In our study we sought to document the CT scan findings in 22 patients with coccidioidal meningitis and to determine whether this test could be used to predict prognosis. The characteristics of these patients with respect to age, sex, race, clinical presentation and evidence of the pathogen in cerebrospinal fluid were similar to those described in other reports on coccidioidal meningitis.

The most common findings were ventricular enlargement together with enhancement or obliteration of the basal cisterns, or both. Ventricular and cisternal abnormalities were usually seen in combination, though one patient had cisternal obliteration with normal-sized ventricles and another had generalized ventriculomegaly with no apparent cisternal changes.

These findings correlate well with known histopathologic changes in patients with coccidioidal meningitis. The fungal organism elicits a granulomatous meningitis with thickening and opacification of the basilar meninges. In later stages of the disease, the meninges around the brain stem may be completely replaced by a thick inflammatory exudate consisting of lymphocytes, plasma cells, multinucleated giant cells and coccidioidal spherules with endospores. Hydrocephalus develops when this inflammatory process produces obstruction in the subarachnoid space at the skull base or in the fourth ventricular outlet foramina.

Inflammation may also extend into the ventricular surface to produce a granular ependymitis. This accounts for the ependymal enhancement seen in one of our patients and probably explains the asymmetric ventricular enlargement seen in eight other patients. Ventriculitis beginning in the posterior fossa could produce complete or partial fourth ventricular obliteration (as it did in four patients) or focal dilatation of the fourth ventricle or temporal horn (seen in four patients), depending on the specific locus of ependymal proliferation. Acquired fourth ventricular enlargement after lateral ventricular shunting was noted in two patients. This has been described by others[7] and is presumably due to obstruction of the Sylvian aqueduct superimposed on a generalized hydrocephalus produced by the coccidioidal basilar exudate. Recognizing this phenomenon is important because a loculated fourth ventricle may act as a posterior fossa mass lesion and require surgical decompression.

Two of our patients had small hypodense areas in the subcortical white matter. Although cerebral angiograms were not obtained, vasculitis and cerebral infarction have been documented[8,9] in patients with coccidioidal meningitis caused by the intense inflammatory response around the vessels at the circle of Willis.

The only previous report describing CT scan findings in a large number of patients with coccidioidal meningitis is that of Dublin and Phillips.[10] Their observations in 15 patients are in agreement with our experience regarding the high incidence of ventriculomegaly and cisternal abnormalities. Only one of their patients had a normal scan and they found white matter lesions in six patients. This contrasts with our series in which six of the patients had a normal scan and two had scans showing hypodense areas in the white matter. These differences may be explained by the timing of CT scanning: in our study a CT scan was done when an initial diagnosis was made rather than later in the course of the disease. Their series also differed from ours in failing to note instances of asymmetric ventricular enlargement, a frequent occurrence in our group of patients.

Tuberculous meningitis,[11,12] meningeal carcinomatosis,[13-15] intracranial cysticercosis,[16] other types of fungal meningitis[17,18] and *Hemophilus influenzae* meningitis[19] have all produced CT scan abnormalities similar or identical to those in cases of coccidioidal meningitis. Although the incidence of hydrocephalus may be slightly greater with coccidioidal meningitis, there are no clear-cut radiographic features that allow this disease to be differentiated from other forms of basilar meningitis on the basis of CT scan findings alone. Such a distinction relies on additional information, including the findings in cerebrospinal fluid specimens, and a history of travel or residence in endemic areas.

A correlation was found between initial CT scan findings in patients with coccidioidal meningitis and their subsequent course. Those with normal scans were likely to have signs and symptoms confined to meningeal irritation, while those with abnormal scans were more apt to have evidence of increased intracranial pressure or impaired mentation. Of greater importance was the fact that patients whose CT scans were normal at the time a diagnosis was established seemed to have a better long-term prognosis than persons with abnormal scans. Only one of six patients (17%) with a normal scan has died and the other five (83%) are living independent lives. In the group with abnormal scans, five died (a 31% mortality rate) and seven (44%) are living independent lives. Currently, cure rates in the two groups cannot be assessed as most patients are still undergoing active treatment and their eventual outcome is unknown. Although follow-up intervals differed and treatment protocols were not standardized, the aforementioned observations indicate that initial CT scan findings in patients with coccidioidal meningitis may provide some insight into their subsequent clinical course.

In conclusion, we believe the CT scan is a useful modality in the diagnosis and follow-up of patients with coccidioidal meningitis. Initial CT scans should be done both with and without contrast enhancement, as this may disclose subtle cisternal or ependymal abnormalities not apparent on unenhanced scans alone. Contrast enhancement can usually be avoided in subsequent studies to assess ventricular size when a diagnosis of coccidioidal meningitis has already been established. Although a normal CT scan does not exclude the presence of coccidioidal meningitis, it does indicate a more favorable prognosis for those who have the disease. Serial CT scans help to select patients who will require ventricular drainage and are essential to identify patients in whom fourth ventricular loculation develops after lateral ventricular shunting.

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Medical Practice Question

EDITOR'S NOTE: *From time to time medical practice questions from organizations with a legitimate interest in the information are referred to the Scientific Board by the Quality Care Review Commission of the California Medical Association. The opinions offered are based on training, experience and literature reviewed by specialists. These opinions are, however, informational only and should not be interpreted as directives, instructions or policy statements.*

Computed Tomography/Multiplanar Reformation

QUESTION:

Is computed tomography/multiplanar reformation an accepted medical practice for the diagnosis of spinal disorders or is it considered investigational?

OPINION:

In the opinion of the Scientific Advisory Panel on Radiology, computed tomography/multiplanar reformation is considered an accepted, but not routine, medical practice for the diagnostic evaluation of lumbar spine disorders. This technique adds valuable information in certain cases of trauma to the spine and in selected other diagnostic situations where transaxial scans are judged inadequate, but it should be used on an individual case basis. It is not suggested as a general approach to a limited disc/radicular pain syndrome that is limited to one level.

In the vast majority of patients, a satisfactory diagnosis of pathologic conditions can be obtained using the usual primary axial images obtained by computed tomography. Finally, it was observed that most modern third and fourth generation computed tomography scanners can provide images comparable to multiplanar reformation images, with some minor exceptions, such as the "curved coronal images."